NewTherapiesSubgroup

Minutes

20Th January 2015, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

GMMMG Greater Manchester Medicines Management Group

NHS

Present:

Elizabeth Arkell (EA), Associate Director of Pharmacy, UHSM Foundation Trust
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Elizabeth Craig (EC) Medicines Information Pharmacist, PAHT
Aoidin Cooke (AC) Medicines Information Pharmacist, CMFT *(deputy for Jane Law)*
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Andrew Martin (AM) Strategic Medicines Optimisation Pharmacist, GM CSU.
Keith Pearson (KP) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Bhavana Reddy (BR) Head of Prescribing Support, RDTC *(Professional Secretary)*
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG
Dr Richard Warren (RW) NIHR Senior Clinical Lecturer and Consultant Dermatologist, Salford Royal Foundation Trust.

Apologies received: HS, D'OR

Declarations of Interest
The following declarations of interest were made which related to the agenda.

- Receipt of hospitality from GSK at launch event for Anoro,
- Receipt of hospitality from BI at tiotropium in asthma launch event
- Advisory board work for AZ for Symbicort.
- Advisory board work for Teva for DuoResp.

These were noted and would be considered when the relevant agenda items were discussed.

1) Minutes of the meeting on December 2014.

The minutes were accepted as a true and accurate record following a few minor typo amendments.

ACTION RDTC to publish as final.

2a) Matters Arising - nabilone for chronic pain draft recommendation

The group discussed the draft nabilone recommendation and agreed that based on the unlicensed indication and very limited clinical evidence of benefit it should not be recommended.

It was agreed that the mechanism for use in exceptional circumstances should be updated to read '*the specialist should have a discussion with the local CCG medicines management lead and/or prescribing lead prior to prescribing'.* The group then went through the criteria for addition to the DNP/Grey/non formulary list and it was agreed that nabilone for chronic pain (unlicensed) should be added to the DNP list as no specific patient group that may benefit could be identified.

ACTION: BR to update recommendation as above then take to GMMMG

2b) Matters arising –Sativex® for non- MS pain draft recommendation

The group discussed the draft Sativex® recommendation and agreed that based on the unlicensed indication with limited clinical evidence of benefit it should not be recommended.

It was agreed that the mechanism for use in exceptional circumstances should be updated to read '*the specialist should have a discussion with the local CCG medicines management lead and/or prescribing lead prior to prescribing'.* The group then went through the criteria for addition to the

DNP/Grey/non formulary list and it was agreed that Sativex® for chronic (non-MS) pain (unlicensed) should be added to the DNP list as no specific patient group that may benefit could be identified.

ACTION: BR to update recommendation as above then take to GMMMG

2c) Matters arising – draft Relvar® recommendations

The group discussed the two separate asthma and COPD recommendations which had now been drafted following discussions at the previous meeting. They also noted the comments from the specialist regarding place in therapy. New data supplied by the manufacturer was also considered. The group was satisfied that the clinical evidence now shows that Relvar® may be a cost effective option for use as below:

- For COPD - as a treatment option in patients with severe COPD (FEV1) <50% predicted normal (post-bronchodilator) with a history of recurrent or severe exacerbations requiring admission or use of rescue treatments despite regular bronchodilator therapy.
- For asthma - as an option for use in asthma patients who have a preference for the dry powder multidose Ellipta® device.

It was noted that the 30-day cost of Relvar 92/22 mcg is £27.80. However other ICS/LABA inhalers may be available at a lower daily cost depending on steroid molecule, dose and device type.

ACTION: BR to update recommendations and take to GMMMG for sign off.

2d) Tadalafil once daily recommendation.

The group reviewed the Tadalafil once daily recommendation and noted that no new evidence had been published since it was last reviewed however generic sildenafil is now available without the SLS specification but also at a much cheaper cost. It was agreed this meant that prescribing tadalafil once daily was no longer cost effective compared to alternative treatments and that this recommendation should be updated as below:

The group does not recommend the use of tadalafil once daily tablets for the above indication.

There is no convincing evidence that any one PDE-5 inhibitor is safer or more effective than any other, therefore generic sildenafil should remain the first line treatment choice. For those patients who have no response to generic sildenafil and meet the 'SLS' requirements then avanafil once weekly is *currently* cheaper than both vardenafil and tadalafil.

One year's treatment costs with tadalafil once daily are £714.87 compared to £15.54 and £250.96 for sildenafil 100mg once a week and avanafil 200mg once a week.

The group agreed that tadalafil once daily would be suitable for the DNP list based on affordability and cost effectiveness however it may be difficult to distinguish between the once daily and the prn preparation which shouldn't be added to DNP.

ACTION: BR to update recommendation as above and take to GMMMG.

3) Duaklir® (aclidinium/formoterol) Genuair® combination inhaler for COPD review

The group considered the clinical evidence for use of Duaklir® inhaler for COPD and noted the following points from the clinical evidence:

- Two almost identical phase III 24-week RCTs were carried out comparing the efficacy of aclidinium/formoterol 340/12 to a lower strength product (340/6 – not licensed), aclidinium alone, formoterol alone and placebo.
- Both trials enrolled patients >40 years with stable moderate to severe COPD according to GOLD criteria and with at least 10-pack years of smoking history. ACLIFORM – COPD enrolled 1729 patients and AUGMENT-COPD enrolled 1692 patients.
- The proportion of patients receiving 340/12 aclidinium/formoterol groups who achieved clinically relevant improvements in transitional dyspnea index and on the St George's respiratory questionnaire was similar to those reported for other LAMA/LABA trials.
- Mean FEV1 across the trials was 52-55% of predicated.
- The pooled rate of moderate to severe exacerbations (assessed as an additional variable) was lower with aclidinium/formoterol 340/12 than with placebo (NNT = 8 to prevent one event per year)

- A year's treatment with aclidinium/formoterol 340/12 will cost £394 which is nearly £100 cheaper than the individual components prescribed separately and £83 cheaper than the cheapest LABA and LAMA inhalers prescribed separately. Duaklir® Genuair® is the same price as Anoro® Ellipta® - another LAMA/LABA combination inhaler.

The New Therapies Subgroup of the GMMMG considered the use of Duaklir® Genuair® (aclidinium/formoterol) 340/12 combination inhaler to relieve symptoms in adult patients with COPD.

The group recommend the combination aclidinium/formoterol inhaler as an option where a separate LABA and LAMA inhaler would be prescribed.

Two phase III trials showed similar clinically relevant improvements as those reported in other LAMA/LABA combination trials. Aclidinium/formoterol 340/12 combination inhaler costs £394 per patient per year. This is cheaper than the cost of separate LAMA and LABA inhalers and may help with adherence for some patients.

According to set criteria for the above indication Duaklir® Genuair® was deemed to be a medium priority for funding.

ACTION: BR to draft recommendation as above

The group evaluated Duaklir® against the formulary criteria and agreed that it should be included in the formulary as another LAMA/LABA combination inhaler. Choice of inhaler would depend on the products prescribed initially and device preference.

ACTION: BR to feed this back to the formulary subgroup

4) Tiotropium for asthma

The group considered the clinical evidence for use of tiotropium as add on maintenance bronchodilator treatment in adult patients with asthma. The group noted the following points:

- Tiotropium is licensed for use in adult patients with asthma who are currently treated with maintenance treatment of an inhaled corticosteroid (>800 µg budesonide/day or equivalent) and long acting β2 agonists who experienced one of more severe exacerbations per year.
- The recommended dosage in asthma is inhalation of 5mcg given as two puffs from the Respimat® inhaler once daily, at the same time of the day.
- The tiotropium (Spiriva® Respimat®) phase III clinical trial programme included two 48 week-treatment duration, randomised, double-blind, placebo-controlled trials in 912 asthma patients, known as the PrimoTin A-asthma studies.
- Trials have demonstrated that tiotropium in asthma may improve lung function compared to placebo, with a side-effect profile similar to that seen in COPD
- However patients included in the trials had long-standing asthma (around 28 years) with late diagnosis (around age 26 on average) which may limit the applicability of the results.
- Actual ICS doses used were not reported and patients at increased risk of anticholinergic AE or CV events excluded from trials which may limit the confidence in the safety data based on previous concerns with Respimat®
- The BTS/SIGN guidelines indicate that a new alternative at step 4 may be the use of long-acting muscarinics, such as tiotropium. However whilst a line has been included to this effect it is important to note that the use of tiotropium in asthma has not been fully reviewed by the current SIGN/BTS guideline and the guidance states that longer term evidence is required to support a recommendation.
- There is no direct comparison data with other options at step 4 (this includes escalation of steroid dose, where appropriate).

The group agreed that tiotropium may have advantages over alternatives at Step 4 of the BTS guidelines in terms of reduced potential for side effects and interactions compared with oral agents such as theophylline and β2 agonist tablets however the position of tiotropium (Spiriva®

Respimat®) in the clinical management of asthma still remains to be established. It was agreed that specialist input should be sought before a definite recommendation is made.

ACTION: BR and PB to contact specialist re: Tiotropium use in asthma patients.

5) Naloxegol for constipation review

The group reviewed the clinical data for the use of naloxegol (Moventig®) a peripherally-acting mu-opioid receptor antagonist for the treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s). The group noted the following points from the clinical trials:

- Naloxegol is indicated for patients with OIC who have had an inadequate response to laxatives, defined as symptoms of at least moderate severity for two weeks despite taking at least one laxative class for a minimum of four days.
- The efficacy and safety of naloxegol in the treatment of OIC have been evaluated in two multi-centre, randomised, double-blind, placebo controlled trials lasting 12 weeks (KODIAC-04 & KODIAC-05).
- Participants (n=1337) had opioid induced constipation, defined as less than 3 spontaneous bowel movements per week along with hard or lumpy stools, straining, or a sensation of incomplete evacuation, or anorectal obstruction in at least 25% of bowel movements during the preceding 4 weeks.
- Both studies compared naloxegol 25mg (n=446) and 12.5mg (n=445) with placebo (n=446).
- Recruited patients were on a stable regimen of opioid analgesics for non-cancer pain only, which does not adequately reflect real-life use of opioids.
- Naloxegol is metabolised by the cytochrome P450 isoenzyme 3A4, which means it has the potential to interact with many drugs.
- The European license is wider than that granted in the US, which specifies that it should be used solely in non-cancer pain patients as per the clinical trials.
- The most commonly reported adverse events in trials were gastrointestinal in nature, including abdominal pain, diarrhoea, nausea, flatulence, and vomiting. However evidence of longer term safety is limited.
- There is no specific UK guidance on the treatment of OIC in non-palliative care patients. Guidance for OIC in palliative care recommends the use of prophylactic laxatives. Expert opinion recommends the use of both osmotic and stimulant laxatives.
- The costs of naloxegol are currently unknown, but they are likely to be higher than standard laxative therapy.

The group agreed that further data was required before naloxegol could be recommended for use, including price and comparison data against existing laxatives.

The New Therapies Subgroup of the GMMMG considered the use of naloxegol for the treatment of opioid induced constipation (OIC) in patients who have an inadequate response to laxatives.

The group does not recommend the use of naloxegol for the above indication.

The group was particularly concerned about:

- The lack of long term safety or efficacy data.
- The lack of comparison data with current standard therapy which includes the use of at least two classes of laxatives prophylactically alongside lifestyle advice.
- The efficacy of naloxegol for the treatment of OIC in patients with cancer pain remains unknown as cancer patients were excluded from the main clinical trials.
- The costs of naloxegol are currently unknown, but they are likely to be higher than standard laxative therapy

According to set criteria naloxegol was deemed to be a low priority for funding

ACTION: BR to draft recommendation as above

It was agreed that naloxegol would be not be recommended for addition to the formulary, DNP or Grey lists but would be discussed again should further data or information be available.

6) Biosimilars

The group had been asked whether they will be reviewing *biosimilars*. Discussion took place around what extra value NTS could add to the already expanded regulatory process. It was agreed that the EMA are experts in assessing bioequivalence so it was unclear what the role of NTS would be in this case.
The group noted the fact that companies do have to carry out a clinical trial to show equivalence with the branded product however once equivalence was proven through the clinical trial then the biosimilar would be granted a license for all indications that the branded product had a license. The group also noted the NICE statement around biological technologies and 'biosimilars' and that NICE would be considering all biosimilars along with the branded product so when a TA needed updating the new TA would apply to the brand and 'branded biosimilars' but that they would be named and considered individually. It was felt that the group may not be able to add anything extra with regards biosimilar biologics as this would depend on specialist input and the EMA license. It was noted that most biosimilar companies will only bring to market a drug that has some advantage over the existing product e.g. lower cost, better administration etc
The group also raised the issue of the insulin products which could be considered as biosimilars. It was felt that some practical advantages around use of these over existing products could be considered and a position statement issued. It was agreed that advice would be sought from GMMMG before a definite decision was made.

ACTION: BR to take to GMMMG for discussion

7) Current work plans & new submissions received since January & Horizon Scanning

The group reviewed the work plan and monthly horizon scanning documents and agreed that naltrexone/bupropion for obesity and Safinamide for Parkinson's should be discussed in February. It was noted that secukinumab and apremilast were now launched and it was felt that these could be discussed in the March meeting depending on NICE timescales.

ACTION: BR to add above drugs to the agenda for February

8) Updates from other groups.

Formulary Subgroup
The group was updated on the last formulary subgroup meeting.
GMMMG
The group noted that had been no GMMMG meeting in January.
Interface Subgroup
The group was updated on the interface subgroup meeting.

9) AOB

No other business was raised.

10) *Date of Next Meeting: 17th February 2015, 12.30-2.30pm, CMFT*